

## **REMARKS**

### **Request for an Update to the USPTO's Electronic Application Data**

In the response filed on September 13, 2007, Applicants requested correction of the Filing Receipt to indicate the priority claim to GB 0229793.5. Applicants note that the Image File Wrapper for this application shows a Bibliographic Data Sheet signed by the Examiner and entered into the file on November 28, 2007 which acknowledges the priority claim. However, the USPTO's electronic application data does not seem to have been updated to reflect the priority claim. Applicants' attempts to prompt correction of the USPTO's electronic application data have apparently been unsuccessful. Applicants would greatly appreciate any assistance the Examiner can provide in prompting OIPE to update the USPTO's electronic application data.

### **Status of the Claims**

Claims 1, 3, 5, 8-10, 14-15, 35-42, and 45 are canceled. Claims 2, 4, 6-7, 11-13, 16-34, 43-44, and new claims 46-52 are pending. Claims 16-17, 28-31, and 33-34 are withdrawn by the Examiner. Claims 2, 4, 6-7, 11-13, 18-27, 32, and 43-44 are examined and new claims 46-52 are added.

### **Support for Amendments**

Claims 2, 4, 6-7, 11-13, 18, 21-25, and 43-44 are amended and new claims 46-52 are added.

Claim 2 is amended to replace the phrase "variants or portions thereof encoding at least one non-ribosomal peptide synthetase which catalyses at least one step of the biosynthesis of safracins" with preferred embodiments according to the invention. For example, support for

2b can be found on page 6, first paragraph, of the application as filed. Support for 2c can be found in claim 6. Support for 2d can be found on page 14. Support for 2e can be found on page 5, last paragraph, and page 14.

Claim 4 is amended to remove the phrase regarding variants or portions thereof, and include c) previously found in claim 6, and include the full complement of part a, b, or c. Support can be found in the claims as originally filed.

Claim 6 is amended to remove the phrase regarding variants or portions thereof. Support can be found in the claim as originally filed.

Claims 7, 18, and 43-44 are amended for grammatical reasons. Support can be found in the specification as originally filed.

Claims 11-13 are amended to include the term “primer” as an embodiment of the invention. Support can be found in the specification as filed, for example at Example 2.

Claims 21-25 are amended to include the term “recombinant” as suggested in the Office Action (page 7, line 1). Support can be found in the specification as filed, for example at pages 6-7.

New claims 46-52 are presented as various embodiments of the invention. Support can be found in the specification as filed, for example at page 26 and page 29.

No new matter is added.

### **Objection to the Specification**

The Office Action maintains the objection to the specification due to informalities in the abstract. However, Applicants believe that the abstract submitted on September 13, 2007, meets the Examiner’s suggestions in that the abstract submitted on September 13, 2007, was

meant to incorporate the language previously suggested by the Examiner. The abstract as submitted on September 13, 2007, is present in the USPTO's image file wrapper. Therefore, Applicants respectfully request clarification and/or withdrawal of the objection.

### **Sequence Listing**

The Office Action requires a statement that the content of the paper copy and the computer readable form of the Sequence Listing submitted on September 13, 2007, are the same. Applicants believe that this statement is no longer being required by the USPTO. See <<<http://www.uspto.gov/cbc/portal/cfs/legal.htm>>>, Section XIII, which states:

If a filer submits a sequence listing (under 37 CFR 1.821(c)) as a text file via EFS-Web in response to a requirement under 37 CFR 1.821(g) or (h), the sequence listing text file must be accompanied by a statement that the submission does not include any new matter which goes beyond the disclosure of the application as filed. However, if the sequence listing text file complies with the requirements of 37 CFR 1.824, the filer need not submit (i) any additional copies of the sequence listing pursuant to 37 CFR 1.821(c) nor (ii) the statement described in 37 CFR 1.821(f).

However, in order to be responsive to the Office Action, a statement is attached.

### **Claim Objections**

Claims 2 and 18 are objected to for various informalities. By amendment, claims 2 and 18 are amended as suggested by the Examiner. Applicants request withdrawal of the objections.

**Rejection Under 35 U.S.C. § 101**

Claims 14 and 15 are rejected under 35 U.S.C. § 101 as directed to non-statutory subject matter. Applicants respectfully traverse. However, in order to advance prosecution, claims 14 and 15 are canceled. Applicants request withdrawal of the rejection.

Claims 21-25 are rejected under 35 U.S.C. § 101 as directed to non-statutory subject matter. Applicants respectfully traverse. However, in order to advance prosecution, claims 21-25 are amended to include the term “recombinant” as suggested by the Office Action. Applicants request withdrawal of the rejection.

**Rejection Under 35 U.S.C. § 112, first paragraph**

Claims 2-15, 18-27, 32, and 43-45 are rejected under 35 U.S.C. § 112, first paragraph for lack of enablement for the entire scope of the claims. The Office Action argues that the amount of guidance is insufficient for purposes of enablement. Applicants respectfully traverse the analysis on the basis that as amended the claims are enable, and for certain purposes where guidance is necessary, the specification does provide sufficient guidance, and alternatively, on the basis that for certain other purposes, the guidance required by the Office Action is not necessary.

With respect to structure and function, the specification provides detailed information on the structure as claimed. For example, Claim 2 specifies SEQ ID NO:1, which is defined in the sequence listing. Sequence information is amenable to computer analysis with commercially-available software, such as DNA-Star, as discussed in the specification at page 24, lines 5-7. Therefore one of skill in the art, with SEQ ID NO:1 in hand, is provided detailed guidance with respect to the structures as claimed.

Regarding conserved regions/domains and predictability of the result of changes in structure, the specification at page 12, lines 17-27 provides detailed information regarding highly conserved regions. Additional information regarding highly conserved regions is provided on page 14, line 8 through page 15, line 5. The detailed information even identifies the activity of various active sites, such as the serine at the “site of thioester formation” at page 14, lines 19-22, and sites of ATP binding and hydrolysis. In addition, the specification provides information from knock-out mutants which provides additional information as to the types of changes that can be tolerated while maintaining activity (see specification, pages 19 and 20, and figures 5 and 6), i.e. due to the modular nature of the gene cluster, modular regions can be removed without affecting the activity of the remaining modular regions. Furthermore, with regard to the Office Action’s requirement for maintaining the desired activity in the encoded protein, claim 2 and the claims which depend from claim 2 include the language wherein the embodiments are specified, and full complements thereof. With regard to the primers or hybridization probes of claims 11-13, Applicants assert that encoding a functional protein is not the intended use and therefore such guidance is not required. Therefore, one of skill in the art is provided with detailed information regarding conserved regions/domains, where such information is necessary.

Claims 2-15, 18-27, 32, and 43-45 are rejected under 35 U.S.C. § 112, first paragraph for lack of written description. The Office Action points to the phrase “at least 30% identity to the peptide”. By amendment, claim 2 includes an embodiment with 95% homology. In addition, the specification fully describes SEQ ID NO:1 as a species within the genus as claimed. Furthermore, the common characteristics of additional species are identified in the claims, including such common characteristics as homology, hybridization, and biological

activity of sequences within the genus (*i.e.* encoding proteins with homology to SEQ ID NOs 2-15). As noted above in the response to the enablement rejection, the specification provides detailed information on the conserved regions and active sites of the gene products, *i.e.* the structure and function of the embodiments of the invention.

**Rejection Under 35 U.S.C. § 112, second paragraph**

Claims 4-5, 11-15, and 43-45 are rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. Upon entry of this paper, claims 5 and 45 are canceled.

Claims 4 and 43-44 are rejected for lack of antecedent basis in claim 2. Upon entry of this paper, claim 2 is amended to provide antecedent basis for claims 4 and 43-44.

Claims 11-15 are rejected due to the phrase “stringent conditions” because the Office Action argues that no conditions are provided in the claims. Applicants believe that the phrase “stringent conditions” is sufficiently definite. The main parameters that influence hybridization have been widely discussed in the literature. For example, see <<  
[http://www.roche-applied-science.com/PROD\\_INF/MANUALS/InSitu/pdf/ISH\\_33-37.pdf](http://www.roche-applied-science.com/PROD_INF/MANUALS/InSitu/pdf/ISH_33-37.pdf)>>, which clarifies that melting point and renaturation of DNA are primarily influenced by temperature, pH, concentration of monovalent cations, and the presence of organic solvents. Hybridization depends on the ability of denatured DNA to re-anneal with complementary strands in an environment below their melting point. The melting point is the temperature at which half the DNA is present in a single-stranded form. Stability of double-stranded DNA is directly dependent on the GC content. As a result, the higher the molar ratio of GC pairs in a DNA segment, the higher the melting point. Because SEQ ID NO:1 is a long sequence, and may have regions of varying GC content, the optimal hybridization conditions with a primer or probe will

vary. For example, the following examples of varying melting points are available for some oligonucleotides hybridizing with different regions of SEQ ID NO:1. The different  $T_m$ 's are determined in part by the GC content.

TTTTTCAGAGCCCCACCGGATG

MW	$T_m$ °C	%GC	Secondary Structure	Dimers	Base Count
6686.3	72.8	54.6	None	No	22

TCAAAACATGCAAAGCGTCGGTA

MW	$T_m$ °C	%GC	Secondary Structure	Dimers	Base Count
7065.6	70.1	43.5	None	No	23

GAAATTTTGAGAACATCATT

MW	$T_m$ °C	%GC	Secondary Structure	Dimers	Base Count
6139.0	53.1	25.0	Very weak	No	20

CGGGGGCCGCACGCTGGATC

MW	$T_m$ °C	%GC	Secondary Structure	Dimers	Base Count
6449.1	83.5	81.0	Moderate	Yes	21

In view of the fact that stringent conditions will vary depending on various factors (that are readily ascertainable), one of ordinary skill in the art would know how to design a primer or hybridization probe in order to be specific (*i.e.* under stringent conditions) for SEQ ID

NO:1, and be able to define the hybridization conditions so that the primer or hybridization probe would be specific.

### **Rejection Under 35 U.S.C. § 102(b)**

Claims 2, 4-10, 18-22, 24-27, 32, and 43-44 are rejected under 35 U.S.C. § 102(b) as being anticipated by Pospiech et al. (Microbiology, vol. 141, pages 1793-1803, February 18, 1999) based on the broad recitation of variant or portion thereof. By amendment, the recitation of variant or portion thereof is removed from the claims. The various claimed embodiments of variants and portions (for example in claim 2, sections c) and d)) are not disclosed by Pospiech. Applicants respectfully request withdrawal of the rejection.

### **CONCLUSION**

Based on the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejections and allowance of this application.

### **AUTHORIZATION**

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **50-3732**, Order No. 13566.105008. In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **50-3732**, Order No. 13566.105008.



Respectfully submitted,  
King & Spalding, LLP

Dated: March 26, 2008

By: /michael willis/  
Kenneth H. Sonnenfeld / Michael A. Willis  
Reg. No. 33,285 / Reg. No. 53,913

Customer Number 65989

**Correspondence Address:**

**King & Spalding**  
1185 Avenue of the Americas  
New York, NY 10036-4003  
(212) 556-2100 Telephone  
(212) 556-2222 Facsimile